“DESIGN AND SYNTHESIS OF NEW HETEROCYCLES BY USING KETENE DITHIOACETALS AND SCREENING OF THEIR BIOLOGICAL PROPERTIES”

SHORT RESUME OF THE PLAN PROPOSED FOR INVESTIGATION FOR PH.D. DEGREE UNDER THE FACULTY OF SCIENCE

To be submitted to

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By

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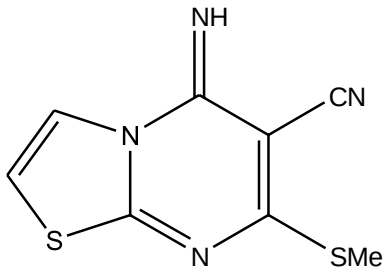
1. Introduction:

Heterocyclic compounds contain at least one heteroatom in their ring. The heteroatom is mostly nitrogen, sulfur, and oxygen. Heterocyclic compounds biologically very important is due to the presence of heteroatoms like (N, O, S). Heterocycles have been found as a key structure in medicinal chemistry and also, and they are frequently found in a large percentage of a biomolecule such as an enzyme, vitamins, and natural products and also show various biological activities including antifungal, anti-inflammatory, anti-bacterial, anti-oxidant, anti-allergic, antituberculosis, anticancer. Due to the broad existence in nature like nucleic acid, hemoglobin, plants, hormones, and enzymes this class is attracted to synthesizing new organic compounds having biological importance. The chemistry of ketene S, S, and N, S acetal as an active area in pull-push alkene which has electron-donating as mercapto SH, alkylthio (S-Me), and cyano as an electron-accepting group at the terminal of C=C double bond. The characteristics of ketene S, S, and N, S acetal make them versatile and easy to use especially in cyclization and multicomponent reactions for the synthesis of various heterocyclic compounds and related natural products particularly derivatives subjected to chemical and biological studies due to their pharmacological activities like an antipyretic, analgesic.

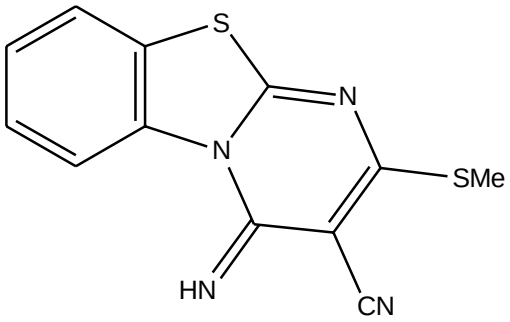
2. Review of literature and development in the subject (Previous work done in the relevant area):

Currently, we are working on the development of the new fused heterocyclic compound by applying new catalytic reagents and some of them have been mentioned below,

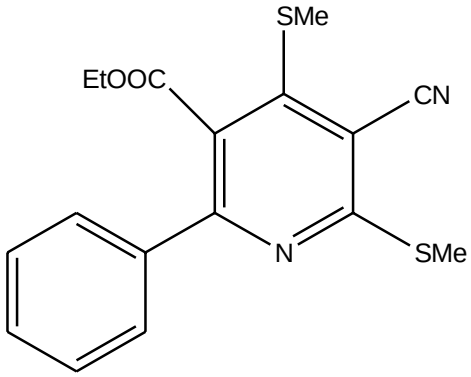
- Ketene S, S-acetals in the synthesis of some new fused pyrimidine derivatives. M.A.Metwally, E.I.Desoky, R. Fawzy and H.A.Etman, Chemistry of the heterocyclic compound, Volume.43, No. 3, 2007.



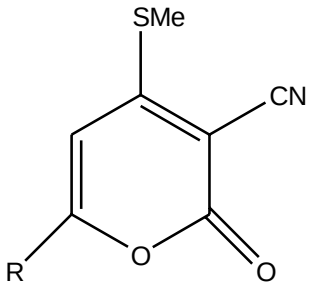
- Ketene S, S-acetals in the synthesis of some new fused pyrimidine derivatives. M.A.Metwally, E.I.Desoky, R. Fawzy and H.A.Etman, Chemistry of the heterocyclic compound, Volume.43, No. 3, 2007



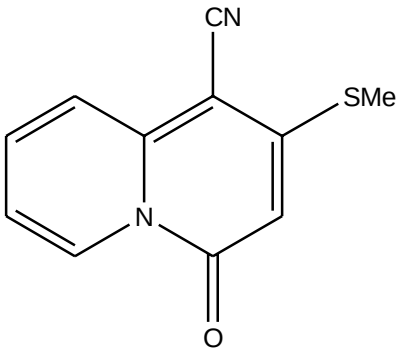
- M. Hagimori et al. / Tetrahedron 63 (2007) 2511-2518.



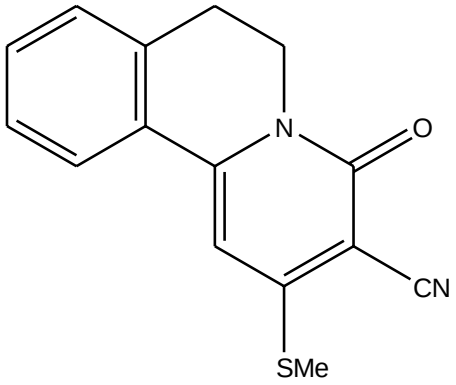
1. Synthesis and Reaction of 6-aryl- and 6-Styryl-3-cyano-4-methylthio-2H-pyran-2-ones Yoshonori Tominaga, Atsuyuki Ushirogochi, Yoshiro Matsuda, and Goro Kobayashi, Chem. Pharm. Bull. 32 (9) 3384 (1984).



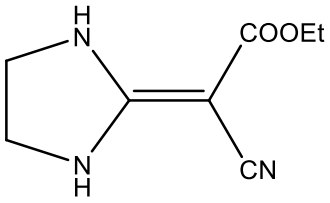
2. Synthesis and Reaction of 1-Cyano-2-methylthio-4H-qunolizine-4-ones., Goro Kobayashi, Yoshiro Matsuda, Reiko Natsuki, Masakatsu Sone., Chem. Pharm. Bull. 20(4) 657-663 (1972).

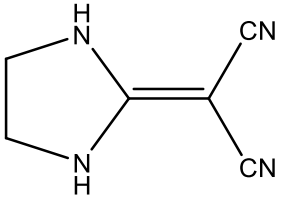


3. Synthesis of 3-Cyano-2-methylthio-4-oxo-6,7-dihydrobenzo[α] quinolizines., Goro Kobayashi, Yoshiro Matsuda, Reiko Natsuki, Masakatsu Sone., Chem. Pharm. Bull. 20(4) 657-663 (1972).

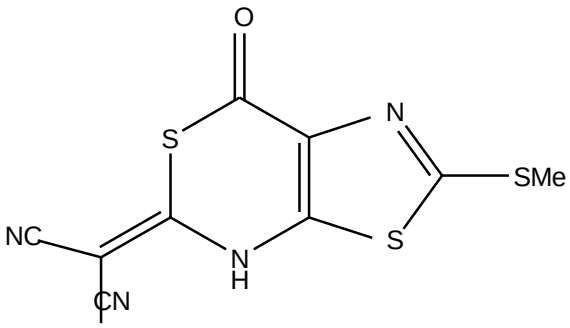


4. Regioselective Synthesis of Heterocyclic Ketene N,N-, N,O- and N,S-acetals in Aqueous Medium.,Langpoklakpam Gellina Chanu, Okram Mukherjee Singh, Sang Hun Jang, and Sang-Gyeong Lee., Bull. Korean Chem. Soc. 2010, Vol. 31, No. 4 859
DOI 10.5012/bkcs.2010.31.04.859

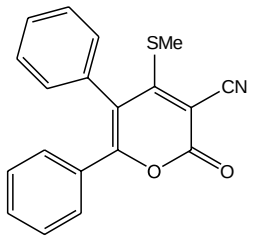




5. Synthesis of Thiazolo[5,4-d]pyrimidine, Thiazolo[5,4-b]pyridine, Thiazolo[4,5-b]pyrrolizine and Thiazolo[5,4-d]thiazaphosphinine, T. I. El-Emary., Phosphorus, Sulfur, and Silicon, 181:1073–1085, 2006.



- Highly Efficient Non-Palladium-Catalyzed Controlled Synthesis and X-ray Analysis of Functionalized 1,2-Diaryl-, 1,2,3-Triaryl-, and 1,2,3,4- Tetraarylbenzenes, Atul Goel, Chem. Asian J. 2007, 2, 239 – 247.



3-substituted-4-(methylthio)-2-oxo-5,6-diphenyl-2*H*-pyran

3. Objectives of Research/ Proposed Hypothesis:

- Synthesis of novel catalytic reagents.
- Extending the research of novel catalytic reagents to the synthesis of different novel imino /oxo fused heterocyclic derivatives.
- Studying mechanistic details of novel catalytic reagents.
- Identify the structure of newly synthesized compounds with help of spectral data.
- Characterization of physicochemical and biological properties of synthesized novel imino /oxo fused heterocyclic compounds.
- Study of molecular modeling and molecular docking of synthesized compounds.

4. Methodology to be adopted:-

- Literature Survey.
- Synthesis and purification of reagent.

- Selection of starting material and synthesis, characterization of different nitrogen containing fused heterocyclic compound by using novel catalytic agent.
- Characterization of newly synthesized heterocyclic compound by using XRD, IR, ^{1}H-NMR, ^{13}C-NMR, Mass spectroscopy.
- Study and evaluation of microbiological activities of synthesized compounds.
- Submission of data to International/National journal for publication.

5. Importance of study/ Society application:

• International Status:

Nitrogen, sulfur, and oxygen-containing fused heterocyclic derivatives help in preventing many viral, fungal and bacterial disease as well as they act as anti-tuberculosis and antioxidant drug with low toxicity. Because of the high efficiency of these compounds following research groups have recognized the importance of this field and made substantial contributions internationally.

1. Yoshinori Tominaga
Faculty of Pharmaceutical Science,
Nagasaki University, Japan.

2. Mona E. Farhan
Department of Chemistry,
Faculty of Science,
Zaazig University, Egypt.

3. Qun Liu
Professor,
Chief Scientist of Speech and Language Computing.
Huawei Noah's Ark Lab, China.

6. National Status:

Heterocyclic compounds such as pyrimidine, pyrazole, imidazole, quinoline, are act as antiviral, antifungal, anti-HIV, anticancer, antioxidant, and anti-inflammatory agents with low toxicity. Because of the high efficiency of these compounds, the following research groups have recognized the importance of this field and made significant contributions nationally.

1. **Vishnu J. Ram**
Division of Medical Chemistry,
Central Drug Research Institute,
Lucknow, India.

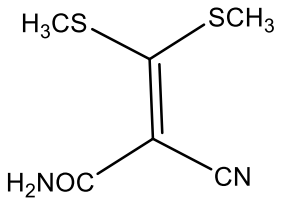
2. **B M Devani**
Associate Professor,
Junagadh Agricultural University, Junagadh,
Gujarat, India.

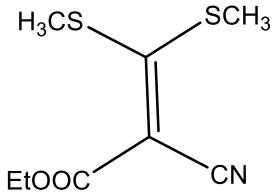
3. **Fateh V Singh**
Assistant Professor, VIT University,
Chennai Campus,
Chennai, India.

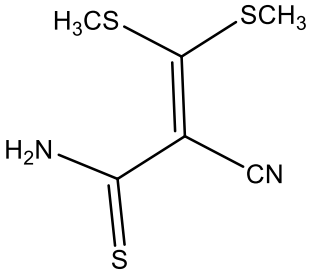
6. Proposed plan/ formulation and structure of study:

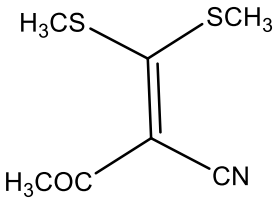
a) Synthesis of amino heterocycles and reagent: (Ist year)

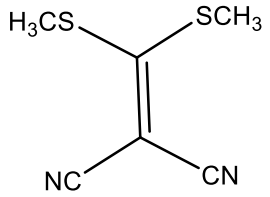
We plan to synthesize different ketene dithioacetal and different substituted amine heterocyclic compounds containing oxygen, sulfur, and nitrogen.

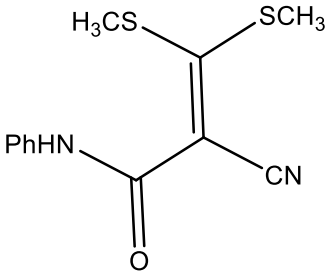


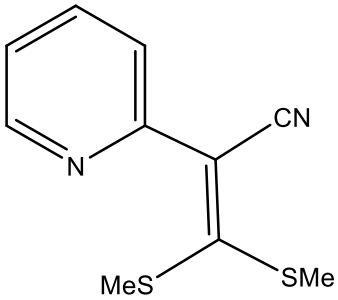


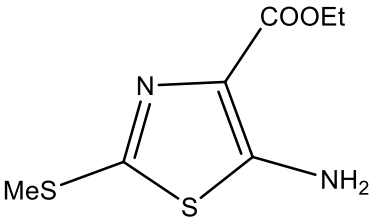




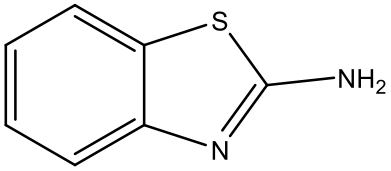




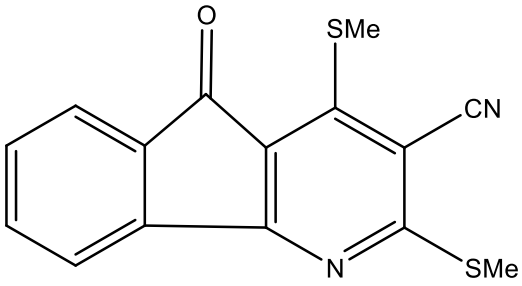




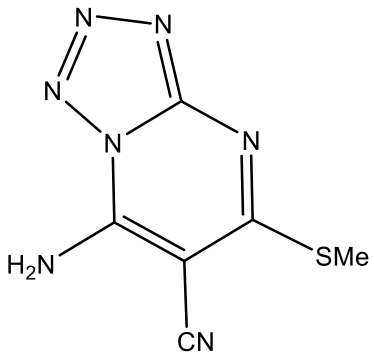
ethyl 5-amino-2-(methylthio)thiazole-4-carboxylate



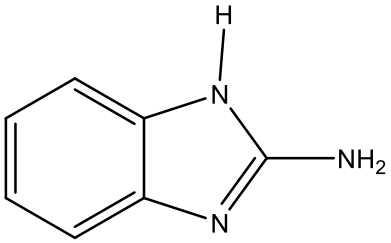
benzo[*d*]thiazol-2-amine



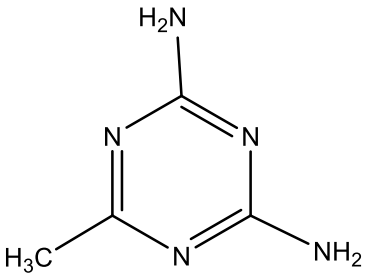
2,4-bis(methylthio)-5-oxo-5*H*-indeno[1,2-*b*]pyridine-3-carbonitrile



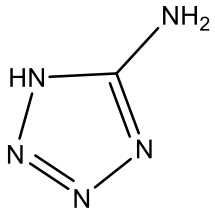
7-amino-5-(methylthio)tetrazolo[1,5-*a*]pyrimidine-6-carbonitrile



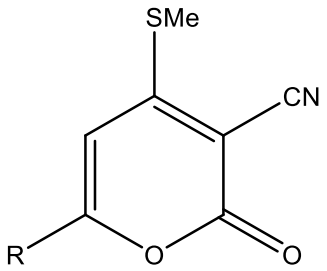
1*H*-benzo[*d*]imidazol-2-amine



6-methyl-1,3,5-triazine-2,4-diamine



1*H*-tetrazol-5-amine



b) Condensation of synthesized amino heterocycle with different reagents: (IInd year)

The synthesized amino heterocyclic compound condenses with reagent to synthesize main heterocyclic compounds. Newly synthesize heterocyclic compound treated with different substituted phenol, aniline, active methylene compound will give new heterocyclic derivatives. Purification of synthesized compound by using crystallization and conformation of structure by using spectral data.

c) Evaluation of Biological Activity: (IIIrd year)

Characterization of newly synthesize heterocyclic compound for pharmacological properties like antioxidant, antimicrobial, antimalarial, antifungal, antituberculosis etc.

Study of Molecular Modeling and Molecular Docking of the newly synthesized compound. Molecular modeling is **an efficient way of studying protein-protein interactions**. It provides detailed information about how protein residues interact with each other at the atomic level. Molecular docking is **a technique that predicts the preferred orientation, affinity, and interaction of a ligand in the binding site of a protein**.

Hence present work title is **"DESIGN AND SYNTHESIS OF NEW HETEROCYCLES BY USING KETENE DITHIOACETALS AND SCREENING OF THEIR BIOLOGICAL PROPERTIES"**

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